TARGETING OF MOLECULES TO LARGE VESSEL ENDOTHELIUM USING EPCR

Abstract of the Invention

Endothelial protein C receptor (EPCR) is found primarily on endothelial cells of large vessels. EPCR translocates from the plasma membrane surface to the nucleus. Molecules which bind to EPCR can be carried from the plasma membrane surface to the nucleus. These molecules include antibodies to EPCR and activated protein C. Protein C, which also binds to EPCR, can be internalized by endothelial cells, but does not enter the nucleus. Thus, EPCR translocation from the plasma membrane to the nucleus provides a means of delivering nucleic acid such as DNA, proteins such as transcription factors, diagnostic agents or other types of drugs to the nucleus of endothelial cells, particularly those on large blood vessels. Conjugates of the materials to be delivered to the nucleus can be formed by ionic or covalent coupling. For example, proteins, including fusion proteins, can be directly conjugated to an anti-EPCR monoclonal antibody. Covalent attachment of positively charged polymers, such as polylysine, to an anti-EPCR antibody allows nucleic acid to bind by ionic charges. Steptavidin and biotin can also be used to conjugate molecules to anti-EPCR antibodies. These conjugated antibodies are transported to the nucleus by EPCR. Eamples demonstrate selective transport to the nucleus which is mediated by EPCR. Molecules transported include activated protein C, antibodies to EPCR, and steptavidin-biotin conjugates. Modification of anti-EPCR monoclonal antibodies by covalently coupling to polylysine allows binding of an expression vector to the modified antibody and translocation to the nucleus.